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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/147,362	03/12/99	CHENEBAUX	D P63163US0

EXAMINER

HM22/0329

JACOBSON PRICE HOLMAN & STERN
400 SEVENTH STREET NW
WASHINGTON DC 20004

PARKIN, J

ART UNIT	PAPER NUMBER
1648	11

DATE MAILED: 03/29/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/147,362	Chenebaux, D.M., et al.
Examiner	**Group Art Unit**
Jeffrey S. Parkin, Ph.D.	1648

☒ Responsive to communication(s) filed on *8 Jan 2001*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *15-30* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *15-30* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4, 7*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☒ Notice to Comply with 37 CFR 1.821-1.825

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Detailed Office Action

Status of the Claims

1. Applicants' election with traverse of the peptidic species having SEQ ID NO.: 14 in paper no. 10 is acknowledged. The traversal is based upon the premise that the claimed peptides all share a common structure and that no objection to lack of unity was raised during the international phase of this application. Applicants' arguments are not deemed to be persuasive. Contrary to applicants' assertion, each peptidic species has a different amino acid sequence with attendant biochemical and immunological properties. Obviously, separate searches will be required for each peptide. Furthermore, applicants are reminded that the International Searching Authority's assessment concerning lack of unity is **non-binding**. If the examiner finds that a national stage application lacks unity of invention under 37 C.F.R. § 1.475 applicants will be required to elect a single group as set forth in the action. As long as the examiner applies those guidelines governing unity of invention, such a requirement is proper. Refer to § 1893.03 of the M.P.E.P. Applicants are further advised that the amendment to the claims set forth in the amendment filed 02 October, 2000, has not been entered. Applicants are required to submit a clean copy of the claims containing the desired amendments. Claims 15-30 are pending in the instant application.

37 C.F.R. § 1.821-1.825

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence

And/Or Amino Acid Sequence Disclosures. Applicants are reminded that all amino acid sequences that fall under the sequence requirements must contain a sequence identifier. For instance, on page 1 of the specification, the peptide VWG... lacks a sequence identifier (see p. 20 as well). Pages 9-16 also contain peptide sequences that lack appropriate sequence identifiers. The claims also reference various peptides without providing the appropriate SEQ ID NOS.: (i.e., see claims 15, 18, 19, 21, 22, and 24). Applicants should review the entire specification, including the claims, and provide any necessary amendments to bring the application into compliance. Any questions regarding compliance with the sequence rules requirements specifically should be directed to the departments listed at the bottom of the Notice to Comply. Failure to comply with these requirements will result in **ABANDONMENT** of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Information Disclosure Statement

3. The information disclosure statements filed 08 December, 1998, and 05 October, 2000, have been placed in the application file and the information referred to therein has been considered.

Disclosure

4. The disclosure is objected to because it is informal in arrangement. The following guidelines illustrate the preferred layout and content for patent applications. each of the lettered items should be preceded by the headings indicated below.

(a) Title of the Invention.

(b) Cross-References to Related Applications (if any).

(c) Statement as to rights to inventions made under Federally-sponsored research and development (if any).

(d) Background of the invention.

1. Field of the Invention.

2. Description of the Related Art including information disclosed under 37 C.F.R. § 1.97-1.99.

(e) Summary of the Invention.

(f) Brief Description of the Drawing.

(g) Description of the Preferred Embodiment(s).

(h) Claim(s).

(I) Abstract of the Disclosure.

Applicants are required to amend the specification to meet these requirements.

37 C.F.R. § 1.72(b)

5. This application does not contain an abstract of the disclosure as required by 37 C.F.R. § 1.72(b). An abstract on a separate sheet is required.

Claim Objections

6. Claims 15, 18, 19, 21, 22, and 24 are objected to because they fail to contain appropriate sequence identifiers (SEQ ID NOS.:) for the recited peptides. For example, claim 15 references the peptide sequences Lys-Gly-Lys-Leu-Ile and Lys-Gly-Lys-Leu-Val without providing appropriate SEQ ID NOS. Applicants are reminded that amino acid sequences consisting of an unbranched sequence of four or more amino acids are subject to the sequence provisions set forth under 37 C.F.R. § 1.821-1.825. Appropriate correction is required.

7. Claims 15 are further objected to because of the following informalities: in claim 15, the sentence "never form ogether the" should read --never form together the--. The claim also lacks antecedent basis for the term Ω_1. Claim 20 lacks antecedent basis for the term Ω_a. Claims 21 and 22 are redundant for reciting the same peptide species more than once in the same claim. Applicants may wish to amend the claim language to simply refer to the appropriate SEQ ID NO.: (i.e., Isolated and purified synthetic peptides selected from the group consisting of SEQ ID NO.: 1, SEQ ID NO.: 2, SEQ ID NO.: 3, etc.). Appropriate correction is required.

35 U.S.C. § 112, Second Paragraph

8. Claims 15-30 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

9. Claim 15 fails to clearly set forth the subject matter being claimed. For instance, the various limitations set forth on page 3 of the preliminary amendment are confusing. The claim provides various definitions for the terms Ω_1 and Ψ, yet also references various other peptides which seem to refer to the original structure (i.e., structure XVI). Do these additional structures represent allowed structures for Ω_1 and Ψ or do they refer to the original peptide structure I? Moreover, the various substitutions and modifications permitted do not appear to meet the sequence length requirements. Applicants should clearly and unambiguously identify the permissible sequence length of any given peptide, the

nature of the claim language (i.e., "open" or "closed"), and the various substitutions, modifications, and/or additions that are permissible for each symbol.

10. Claim 20 is vague and indefinite because it lacks antecedent basis for the terms Z_a and Ω_a. Appropriate clarification is required.

11. Claims 27 and 28 are vague and indefinite for failing to clearly set forth the claimed methodology and appropriate steps. The claims simply recite an immunoassay method without providing any additional guidance. The claims also fail to clearly set forth appropriate assay steps (i.e., WB, ELISA, Ag capture, Ab capture, etc.). Appropriate correction is required (i.e., An immunoassay method for the detection of HIV-1 type O-specific antibodies comprising the following steps: 1) obtaining a patient sample suspected of containing HIV-1-specific antibodies; 2) contacting said sample with an antigen comprising an immobilized peptide according to claim 15 under conditions that permit the formation of an antigen-antibody complex; 3) removing any non-specifically bound antibody through repeated washes; 4) detecting the formation of said antigen-antibody complex by admixing a labeled antibody specific for patient antibodies; etc.).

12. Claims 29 and 30 are vague and indefinite for failing to clearly set forth the purpose of the kit and those reagents necessary to complete the diagnostic assay. Appropriate correction is required (i.e., A diagnostic kit for the detection of HIV-1 type O-specific antibodies comprising the following: 1) a container comprising a synthetic peptide according to claim 1; 2) a container comprising a labeled antibody for the detection of peptide-antibody complexes; 3) a container comprising a buffer to remove unbound antibody; etc.).

35 U.S.C. § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 15, 18, 20, 23, and 25-30 are rejected under 35 U.S.C. § 102(b) as being anticipated by Charneau *et al.* (1996). This teaching discloses various synthetic peptides that appear to meet all the claimed limitations (i.e., see p. 23 wherein the peptide LNLWGCRGKAICYTSVQWNETWG is disclosed). Immunoassay methods and diagnostic kits including this peptide are also provided, as well as, compositions comprising this peptide and other recombinant peptides.

35 U.S.C. § 103(a)

15. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

17. Claims 15, 20, 23, and 25-30 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Brust *et al.* (1998). Brust and colleagues provide antigenic peptides derived from the HIV-1 isolate MVP5180/91. Specifically, the inventors disclose a peptide (MVP601-623) having the amino acid sequence NQQRLNLWGCKGKLICYTSVKWN. This peptide appears to differ from the claimed invention by only two amino acid residues at the carboxyl terminus. While the claimed invention includes AA_7-AA_8 at the carboxyl terminus, the peptide of this teaching omits them. However, the authors state that they have identified a critical epitope in this region corresponding to XKGKLIX, which is present in both peptides. Diagnostic methods and kits employing the peptide, as well as, other type O peptides are also provided. Therefore, the peptide of the '634 patent appears to be an obvious variant of the claimed invention. It contains the same critical motif claimed by applicants (e.g., WGC-Φ-CYTS) and would reasonably be expected to display the same antigenic and immunologic properties as the claimed invention, absent evidence to the contrary. Brust and colleagues also state that additional amino acids may be added to either end of the peptide to provide additional functions (i.e., to facilitate the binding of the

peptide to a solid surface). Thus, it would have also been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to modify the peptide of Brust *et al.* (1998) to include additional amino acids (i.e., X-Ser/Thr) at the carboxyl terminus to facilitate the linking of the peptide to a solid support.

35 U.S.C. § 112, First Paragraph

18. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

19. Claims 15-30 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claims are broadly directed toward synthetic peptides comprising the core motif Trp-Gly-Cys-Φ-Cys-Tyr-Thr-Ser varying in length between 13-33 and 26-66 amino acids depending upon the oligomeric form of the peptide (i.e., monomeric or dimeric). The claims potentially encompass tens-of-thousands of peptides. However, the specification only provides a small number of peptides (e.g., see claims 21 and 22) with minor variations in amino acid sequence. Appropriately drafted claim language directed toward these embodiments would be acceptable (i.e., An isolated and purified synthetic peptide selected from the group of peptides having SEQ ID NO.: 1, SEQ ID NO.: 2, SEQ ID NO.: 3, etc.). However, the disclosure does not support the exceedingly large breadth of the claims.

The legal considerations that govern enablement determinations pertaining to undue experimentation are disclosed in *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988) and *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The prior art is unpredictable and teaches that single amino acid changes, as well as, the addition or deletion of flanking regions, in any given peptide can abrogate antigen-antibody binding interactions (Alexander *et al.*, 1992; Schoofs *et al.*, 1988). For instance, Alexander and colleagues noted that "protein antigenicity can be significantly reduced by alteration of single critical residues." Such substitutions probably induce local changes in the epitope that lead to steric collisions thereby hindering antibody recognition and binding. The disclosure fails to provide adequate guidance pertaining to those substitutions that are permissible and retain the antigenicity of the peptide.

2) The disclosure fails to provide adequate guidance pertaining to the molecular determinants modulating the antigenic characteristics of the claimed peptides. In order to make the various substitutions encompassed by the claims, the skilled artisan would require a knowledge of the epitopic molecular determinants. In the absence of sufficient guidance pertaining to this issue, undue experimentation would be required to ascertain all the various substitutions that would be permitted.

3) The disclosure only provides a small number of working embodiments involving a small number of closely related peptides. The disclosure fails to provide any additional working embodiments or sufficient guidance pertaining to acceptable substitutions.

4) The claims are of excessive breadth and encompass an exceedingly large genus which is inadequately supported by the disclosure. The claims encompass a large genus of compounds, however, as noted *supra*, the disclosure fails to provide sufficient guidance pertaining to the identification of critical molecular determinants and acceptable amino acid substitutions. The unpredictability of the prior art provides another hurdle for the skilled artisan to overcome.

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation to practice the claimed invention in a manner commensurate in scope with the claims.

Correspondence

20. Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward one of the following Group 1600 fax numbers: (703) 308-4242 or (703) 305-3014. Informal communications may be submitted directly to the Examiner through the following fax number: (703) 308-4426. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

21. Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (703) 308-2227. The examiner can normally be reached Monday through Thursday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, James Housel or Laurie Scheiner, can be reached at (703) 308-4027 or (703) 308-1122,

respectively. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

22 March, 2000

Application No.: 09/147,362

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- [ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [X] 7. Other: see paragraph 2 of the Office action

MAY NEED TO

Applicant ~~Must~~ Provide:

- [X] An ~~initial or~~ substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An ~~initial or~~ substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE